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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/046,575 | 01/16/2002 | Nishizumi Nishimuta | 018995-452 | 4939 |

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| EXAMINER | |
|---|---|
| FAY, ZOHREH A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1612 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/046,575 | NISHIMUTA ET AL. | |
| | Examiner | Art Unit | |
| | ZOHREH A. FAY | 1612 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 13-30* is/are pending in the application.

4a) Of the above claim(s) *15-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/2/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 2, 2010 has been entered.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 13, 14 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (WO 98/27960) in view of Fleischer (1999, abstract only); or Fleischer (1999) and Miller et al. (1980, abstract only) and further over the Canadian Patent 2161737 (Submitted by the applicant).

Goodman et al. teach a viscous hydrogel composition containing nitroimidazole (e.g. tinidazole) for treating inflamed skin disease such as rosacea and eczema, see the abstract and page 1, lines 12-15, especially example 1. The specie, tinidazole is well taught and encompassed by scope of the claims.

Applicant's claims differ from WO patent because they specifically require treatment of atopic dermatitis and the concentrations of active ingredients. However, it would have been obvious to a person skilled in the art to substitute the inflamed skin diseases of WO with atopic dermatitis when WO is taken in view of Fleischer (199) or Fleischer and Miller (1980) together because later references, teach deficiencies in Goodman et al.'s teaching. Fleischer teaches that atopic dermatitis is a form of eczema. Fleischer also teaches that immune regulation plays an important role in the cause of atopic dermatitis. Miller teaches that tinidazole is effective immunosuppressant in vivo. See the abstract. The Canadian patent teaches the use of

a topical formulation of metronidazole at the concentrations of 1% cream, 0.75% topical gel and 5% topical suspension for the treatment of inflammatory skin conditions. See Page 1. The above reference makes clear that metronidazole has been previously used at the claimed range concentrations. Applicant's attention is directed to In re Aller, 105 USPQ 233, 220 F2d 454. "Normally, change in temperature, concentration, or both, is not patentable modification; however, such changes may impart patentability to process if ranges claimed produce new and unexpected result which is different in kind and not merely in degree from results of prior art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if modification was within capabilities of one skilled in art; more particularly, where general conditions of claim are disclosed in prior art, it is not inventive to discover optimum or workable ranges by routine experimentation."

Thus, one skilled in the art would have been motivated to prophylactically treat atopic dermatitis using tinidazole, because treating eczema could prevent further undesirable implications (e.g. relapsing or transforming into chronic eczema) which can become atopic dermatitis, considering that tinidazole is proven to be an effective therapeutic modality for eczema or other inflamed skin diseases. If immune regulation were considered to be the underlying mechanism of atopic dermatitis, one would have been motivated to make such substitution with the assurance of reasonable expectation of success, considering that Miller teaches that tinidazole as an effective immunosuppressant in vivo.

One would have been motivated to do so, with the reasonable expectation of success, because it is considered to be desirable to have extended therapeutic modalities to improve patient compliance by enhancing patient satisfaction and increasing the selection option.

These references are particularly pertinent and relevant, because all the claimed species and their roles are well taught in the cited references when they are combined together. Thus, one would have been motivated to combine these references and make the modification because they are drawn to the same technical fields (constituted with the same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. See MPEP 2141.01 (a).

**Response to Argument**

Applicant's arguments and declaration have been carefully considered, but are not deemed to be persuasive. Applicant in his remarks refers to WO'817 trying to establish that there are different types of eczema. The arguments are noted, however such arguments will not overcome the prior art rejection. The prior art clearly teaches that the claimed compounds have been previously used for the treatment of eczema in general. Fleischer et al. teach that atopic dermatitis is a form of eczema. Fleischer et al. also teach that immunosuppressant agents are effective in treating atopic dermatitis. Thus, it would have been obvious to a person skilled in the art to use a compound being used for the treatment of eczema in general and use it for the treatment of atopic dermatitis. The fact that WO'817 teaches that the claimed compounds have been previously used for the treatment of one type of eczema does not mean that it cannot be

used for the treatment of any other types of eczema or atopic dermatitis. In conclusion: Goodman et al. teach the use of the claimed compounds for the treatment of eczema. Fleischer et al. teach that atopic dermatitis is a form of eczema, and immunosuppressant agents, such as tacrolimus can be used for the treatment of atopic dermatitis. Miller et al. teach that tinidazole has immunosuppressive activity. It would have been obvious to a person skilled in the art to use the claimed compounds for the treatment of atopic dermatitis, considering that the prior art teaches atopic dermatitis is a form of eczema and eczema has been treated by the claimed nitroimidazole compounds. The addition of the secondary compounds, such as immunosuppressant agents to the composition of primary reference, would have been obvious to a person skilled in the art considering that Fleischer et al. teach immunosupressent compounds, such as tacrolimus have been previously used for the treatment of atopic dermatitis. The combination of ingredients with the same character is merely the additive effect of each individual component. The Canadian Patent is relied upon to teach that metronidazole has been previously used at the claimed range concentrations for the treatment of inflammatory skin conditions. Applicant's declaration is related to the atopic dermatitis and rosacea, their differences and different treatments have been noted and reviewed, but does not overcome the obviousness rejection

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZOHREH A. FAY whose telephone number is (571)272-0573. The examiner can normally be reached on Monday to Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ZF
/Zohreh A Fay/
Primary Examiner, Art Unit 1612